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EXAMINER

BARTON, JEFFREY THOMAS

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/049,245

Applicant(s)

KAHL ET AL.

Examiner

Jeffrey T. Barton

Art Unit

1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 June 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☒ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 20020708.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☒ Other: Non-patent reference.

## DETAILED ACTION

### *Drawings*

1. The drawings are objected to because Figure 2 contains a label in the German language (Abstand). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### *Specification*

2. The disclosure is objected to because of the following informalities:

- a. On page 1, at line 5, "oligomere" appears where "oligomers" was apparently intended.

Art Unit: 1753

b. On page 11, at line 20, "marcomolecules" appears where "macromolecules" was apparently intended.

c. On page 13, at line 28, and page 14, at line 2, "dye" appears where "die" was apparently intended.

Appropriate correction is required.

### ***Claim Objections***

3. Claims 1, 2, 15, 16, 21, 29, 32, 40, and 44 are objected to because of the following informalities:

a. In claims 1, 16, 21, and 29, in the sixth (1, 16) or fifth (21, 29) paragraph, the word "forces" appears when "force" was intended, and "structures" appears when "structured" was intended.

b. In claims 2 and 15, the phrase, "one of lipids" appears when "one lipid" was apparently intended.

c. In claims 32 and 44, the word "charges" appears when "charged" was apparently intended.

d. In claim 40, it is not clear what is meant by the electrodes "longitudinally expanding in the direction of the channel". Are the electrodes widening, or configured at an angle to the channel?

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11, 28, 33, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding claims 11 and 28, insufficient explanation is given in the specification regarding how a die can be used to provide structures on the substrate having a height as small as 0.1 nm. (i.e. the diameter of a hydrogen atom)

Regarding claims 33 and 45, insufficient explanation is given in the specification regarding how electrophoresis can be carried out on a dry lipid bilayer membrane, without the membrane being specifically rehydrated. The claim is treated herein as though the membrane is dried, then rehydrated.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1753

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 4, 5, 9, 11, 17, 21-26, 28, 29, 31, 32, 34-39, 41, 43, 44, and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Boxer et al.

Addressing claim 1, Boxer et al disclose a method for electrophoretically separating particles, comprising: applying the particles to be separated on a substrate-supported membrane such that the particles are mobile across the surface of the membrane (Column 20, lines 22-49); providing an electric field oriented along the membrane surface (Column 20, line 49-55); and using a substrate-supported membrane having a structured surface such that a force is acting on the particles that leads to movement depending on the length of the particle. (Column 19, lines 20-57)

Addressing claim 21, Boxer et al disclose a substrate used in their method comprising an optically transparent material. (Column 7, lines 21-25)

Addressing claim 29, Boxer et al disclose a substrate supported membrane used in their method comprising a substrate of transparent material and a fluid lipid membrane. (Column 3, lines 28-55)

Addressing claim 35, Boxer et al disclose a microchannel electrophoresis chamber used in their method comprising a channel having a bottom surface comprising transparent material and an electrode assembly. (Column 3, lines 41-46;

Art Unit: 1753

Column 20, lines 49-51; Figure 5 shows electrodes; "coverslip sandwich" meets requirements for a microchannel)

Addressing claims 4, 31, and 43, Boxer et al disclose the membrane comprising amphiphilic macromolecules (Column 7, lines 38-40)

Addressing claim 5, 32, and 44, Boxer et al disclose the membrane comprising bilayers of charged lipids. (Column 22, lines 18-31)

Addressing claims 9, 25, and 26, Boxer et al disclose using a structured substrate comprising ribs to support the membrane. (Figure 1, 28; Figures 2 and 5)

Addressing claims 11 and 28, Boxer et al disclose the height of the ribs being as low as a few nanometers. (Column 5, lines 59-61)

Addressing claim 17, Boxer et al disclose separation of nucleic acids and proteins. (Column 12, lines 12-21)

Addressing claim 22, Boxer et al disclose the substrate being glass. (Column 7, lines 21-25)

Addressing claim 23, Boxer et al disclose plastic being the transparent material. (Column 7, lines 21-25)

Addressing claim 24, Boxer et al disclose the plastic being PMMA (Column 9, line 66 - Column 10, line 11)

Addressing claim 34, Boxer et al disclose the membrane comprising a fluid area. (Column 7, lines 35-40)

Addressing claim 36, Boxer et al disclose a channel width of 1 cm. (Column 8, lines 43-52)

Addressing claim 37, Boxer et al disclose the channel depth ranging from a few nanometers to a few microns. (Column 5, lines 59-61)

Addressing claim 38, Boxer et al disclose a plurality of channels being provided in a two-dimensional matrix (Figure 5; channels between barrier sections 78)

Addressing claim 39, Boxer et al disclose the electrode assembly comprising two electrodes at each longitudinal end of a channel. (Column 20, lines 49-54)

Addressing claim 41, Boxer et al disclose their substrate being coated with a fluid lipid membrane. (Abstract; Column 7, lines 35-40)

Addressing claim 46, Boxer et al disclose the membrane comprising non-fluid areas. (Figure 1; portions above barrier material are not coated)

8. Claims 35 and 40 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Groves et al.

Addressing claim 35, Groves et al disclose a microchannel electrophoresis chamber comprising at least one channel having a bottom surface including a substrate that comprises an optically transparent material (Figure 2A; coverslips used to form the channel; Figure 2B; depth of channel in the tens of microns); and an electrode assembly. (Figure 2A)

Addressing claim 40, Groves et al disclose the two electrodes becoming progressively closer to the channel over most of their length, which can be described as "longitudinally expanding in the direction of the channel." (Figure 2A)



***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Raguse et al.

Boxer et al disclose a method as described above in addressing claim 1. They also disclose their method being able to use membranes formed of any bilayer-forming amphiphile. (Column 7, lines 38-40)

Boxer et al do not explicitly disclose their method using lipids activated by PEG or DAX-Chol lipids for the membrane.

Raguse et al disclose preparation of lipid bilayer membranes using a polyethylene glycol head group. (Column 3, lines 25-38; Column 17, lines 30-34)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by using bilayers comprising lipids with polyethylene oxide head groups, as taught by Raguse et al, because Raguse et al teach their ability to form bilayers, and Boxer et al suggest the use of any bilayer-forming lipids in their method.

12. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al and Raguse et al as applied to claim 2 above, and further in view of Bailey et al.

Boxer et al and Raguse et al disclose a combined method as described above in addressing claim 2.

Neither Boxer et al nor Raguse et al explicitly disclose their method using bilayers comprising cationic lipids.

Bailey et al disclose preparation of liposomes comprising bilayers including cationic lipids. (Abstract)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Boxer et al and Raguse et al by using bilayers comprising cationic lipids, as taught by Bailey et al, because Bailey et al teach their ability to form bilayers, and Boxer et al suggest the use of any bilayer-forming lipids in their method.

13. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Allington.

Boxer et al disclose a method as described above in addressing claim 1. They also disclose the similarity of the separation characteristics of one embodiment of their invention to gel electrophoresis. (Column 19, lines 51-57)

Boxer et al do not explicitly disclose their method using a pulsed electric field (Claim 6), a time constant field superimposed on an alternating field (Claim 7), or the fields of claim 7 being superimposed in a crosswise manner. (Claim 8)

Allington discloses gel electrophoresis methods in which a pulsed electric field is used (Title, Abstract), and a perpendicular alternating field is superimposed on a constant field. (Page 15, lines 3-26)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by using pulsed electric fields or perpendicular superimposed alternating and constant electric fields, as taught by Allington, because Boxer et al disclosed that his method resembles gel electrophoresis

in size-based separations, and such pulsed fields would aid in separating larger macromolecules.

14. Claims 10, 13, and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Austin et al.

Boxer et al disclose a method as described above in addressing claims 9 and 26. They also disclose the ability of their preparation methods to provide features on the nanometer scale. (Column 11, lines 8-12)

Boxer et al do not explicitly disclose the preparation of substrates having structure periodicity of 2-200 nm. (Claims 10 and 27)

Relevant to claims 10 and 27, Austin et al disclose a device suitable for electrophoretic fractionation, which has substrate structures having a periodicity as low as 10 nm. (Column 11, lines 23-27; Figures 3-4A)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by preparing structures in the substrate with periodicity as low as 10 nm, as taught by Austin et al, because Boxer suggested the ability to prepare structures on the nanometer scale, and it would provide the ability to separate smaller molecules.

Furthermore, regarding claim 13, it is obvious that upon migration and contact with a barrier such as those disclosed by Boxer et al or Austin et al, any molecule with a degree of asymmetry will be caused to rotate to some degree.

15. Claims 12, and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Wiktorowicz et al.

Boxer et al disclose methods as described above in addressing claims 1 and 9. They also disclose the similarity of the separation characteristics of one embodiment of their invention to gel electrophoresis. (Column 19, lines 51-57)

Boxer et al do not explicitly disclose their method using an electric field parallel to ribs on the substrate (Claim 12), nor do they disclose any pH gradients in their methods (Claims 18-20)

Wiktorowicz et al disclose electrophoresis methods (primarily gel, but open to others, as indicated by "separation medium" language) in which an electric field is applied parallel to ribs in the substrate. (Figures 3-5; Column 6, lines 39-50) They also disclose electrophoresis methods using pH gradients parallel to the electric field (Isoelectric focusing, Column 8, line 61 - Column 11, line 10) and perpendicular to the electric field (Second dimension after IEF or first dimension before IEF) (Column 15, lines 11-43)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by using an electric field parallel to ribs in the substrate, as taught by Wiktorowicz et al, it would allow analysis of multiple parallel samples in a single run.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by incorporating an immobilized pH gradient on a substrate surface in one dimension of a two-dimensional separation,

as taught by Wiktorowicz et al, because it would provide a useful prefractionation in the separation of complex mixtures.

16. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Groves et al.

Boxer et al disclose a method as described above in addressing claim 1. They also disclose exclusion areas, delineated by the bilayer barrier materials (Column 7, lines 12-19; Figure 1)

Boxer et al do not explicitly disclose collecting particles at the exclusion area upon application of an electric field prior to separation (Claim 14), nor do they disclose observing the separation by recording digitized image data of the separation and evaluating the data using a computer (Claim 16), or the electrode assembly comprising two electrodes longitudinally expanding in the direction of the channel at both sides of each channel. (Claim 40)

Relevant to claim 14, Groves et al disclose the electrophoretic migration of proteins into "corrals" scratched into the substrate surface of a similar device. (Figure 5; Page 2720-2721)

Relevant to claim 16, Figure 4 shows recorded image data, further described by graph insets that were made by computer.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by concentrating analytes in

exclusion areas on the substrate prior to analysis, as taught by Groves et al, because it would provide more effective separation, as in known stacking procedures.

It would also have been obvious to modify the method of Boxer et al by recording image data of the separations and evaluating the data by computer, as taught by Groves et al, because it would provide a complete and efficient means of evaluating the separation.

17. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al and Groves et al as applied to claim 14 above, and further in view of Raguse et al.

Boxer et al and Groves et al disclose a combined method as described above in addressing claim 14. Boxer et al also disclose their method being able to use membranes formed of any bilayer-forming amphiphile. (Column 7, lines 38-40)

Neither Boxer et al nor Groves et al explicitly disclose their method using lipids activated by PEG or DAX-Chol lipids for the membrane.

Raguse et al disclose preparation of lipid bilayer membranes using a polyethylene glycol head group. (Column 3, lines 25-38; Column 17, lines 30-34)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Boxer et al and Groves et al by using bilayers comprising lipids with polyethylene oxide head groups, as taught by Raguse et al, because Raguse et al teach their ability to form bilayers, and Boxer et al suggest the use of any bilayer-forming lipids in their method.

Art Unit: 1753

18. Claims 30, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Bailey et al.

Boxer et al disclose a method as described above in addressing claims 1, 29, and 41. They also disclose their method being able to use membranes formed of any bilayer-forming amphiphile. (Column 7, lines 38-40)

Boxer et al do not explicitly disclose their method using bilayers comprising cationic lipids.

Bailey et al disclose preparation of liposomes comprising bilayers including cationic lipids. (Abstract)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by using bilayers comprising cationic lipids, as taught by Bailey et al, because Bailey et al teach their ability to form bilayers, and Boxer et al suggest the use of any bilayer-forming lipids in their method.

19. Claims 33 and 45 rejected under 35 U.S.C. 103(a) as being unpatentable over Boxer et al in view of Van Wie et al.

Boxer et al disclose a method as described above in addressing claims 29 and 41. They also disclose their method being able to use membranes formed of any bilayer-forming amphiphile. (Column 7, lines 38-40)

Boxer et al do not explicitly disclose their method using previously dried lipid membrane.



Van Wie et al disclose preparation of lipid bilayer membranes for use in sensors, including a step of drying the membrane. (Column 10, line 65 - Column 11, line 11)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Boxer et al by using reconstituted, formerly dried bilayers, as taught by Van Wie et al, because Van Wie et al teach this method of forming bilayers, and Boxer et al suggest the use of any bilayer-forming lipids in their method. It also would facilitate transport of device materials.

### ***Conclusion***

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

Application/Control Number: 10/049,245


Page 17

Art Unit: 1753

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JTB

September 28, 2004



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